

Emergence of sublineages and recombination events: Genetic evolution of SARS-CoV-2

13 de abril de 2022

The occurrence of mutations is a natural and expected event within the evolutionary process of viruses. Since the initial genomic characterization of SARS-CoV-2, this virus has been divided into different genetic groups or clades. In fact, some specific mutations define the viral genetic groups (also called lineages) that are currently circulating globally. Due to various microevolution processes and selection pressures, some additional mutations may appear, generating differences within each genetic group (called variants).

Since January 2020 more than 100 SARS-CoV-2 variants have been identified and only 5 of them have been considered as variant of concern (VOC)¹: Alpha, Beta, Delta, Gamma and more recently Omicron.

After its emergence by mid-November 2021, the Omicron VOC it has rapidly increased in prevalence and became the predominant variant worldwide. In fact, almost 99% of the sequences shared since November 2021 on the GISAID global database correspond to Omicron.

In the Americas, Omicron was first detected by the end of November 2021, and rapidly spread to become predominant in the entire Region. As of April 12, Omicron has been officially reported in 53 Countries and Territories and has been detected in 100% of the samples sequenced in the last 4 weeks.

As expected, the highly transmission pattern demonstrated for Omicron has facilitated the occurrence of additional mutations driving the emergence of different sublineages classified into the same variant (i.e., Omicron). So far (April 12), five (5) different main sublineages of Omicron classified as BA.1 (including BA.1.1), BA.2, BA.3, BA.4 and BA.5 have been reported globally.

Although BA.2 is predominant in most of the Regions at global level (Africa, Asia, Europe, Oceania), in the Americas the sublineages BA.1 and BA.1.1 are still predominant and have been identified in more than 97% of the characterized samples since Omicron introduction. However, the proportions of BA.2 have been increasing in all subregions (**Figure 2**) and in the last four weeks (March 13 – April 9) it represents 35% of the Omicron samples in Latin America (50% in North America).

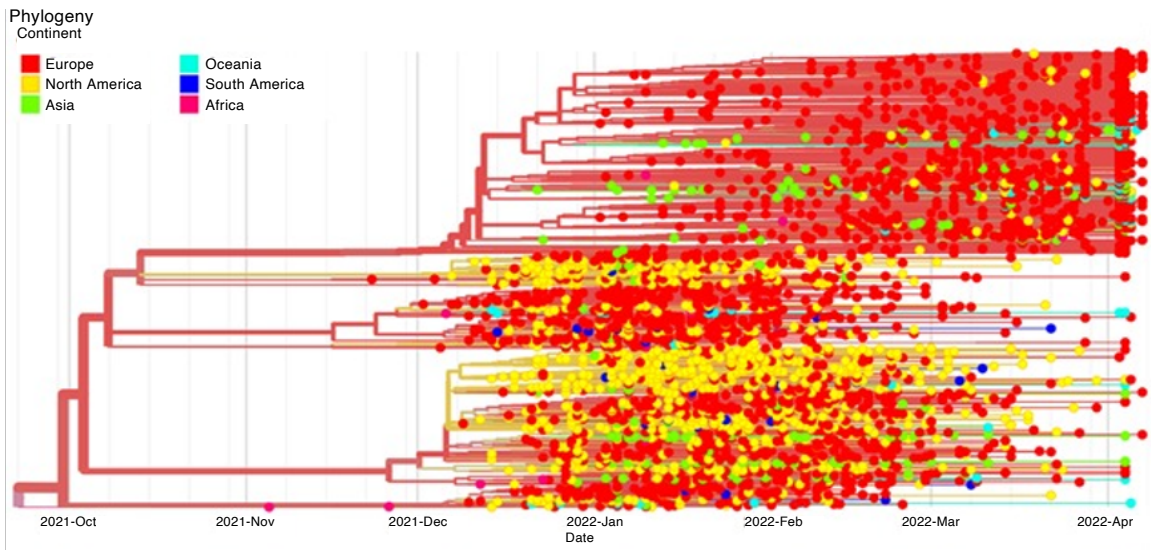
The most recently described sublineages BA.4 and BA.5 were first reported on April 04 in South Africa and have apparently been circulating since January 2022. So far, around 135 Omicron BA.4 / BA.5 sequences have been reported to GISAID database, reported from South Africa (121), Botswana (3), Denmark (6), Germany (2), United Kingdom (2), and Belgium (1).

BA.4 and BA.5 sublineages share a similar Spike (S) protein gene profile as BA.2, except for some additional mutations (69-70del, L452R, F486V) including one similar to the original wild type index virus identified at the end of 2019 (Q493).

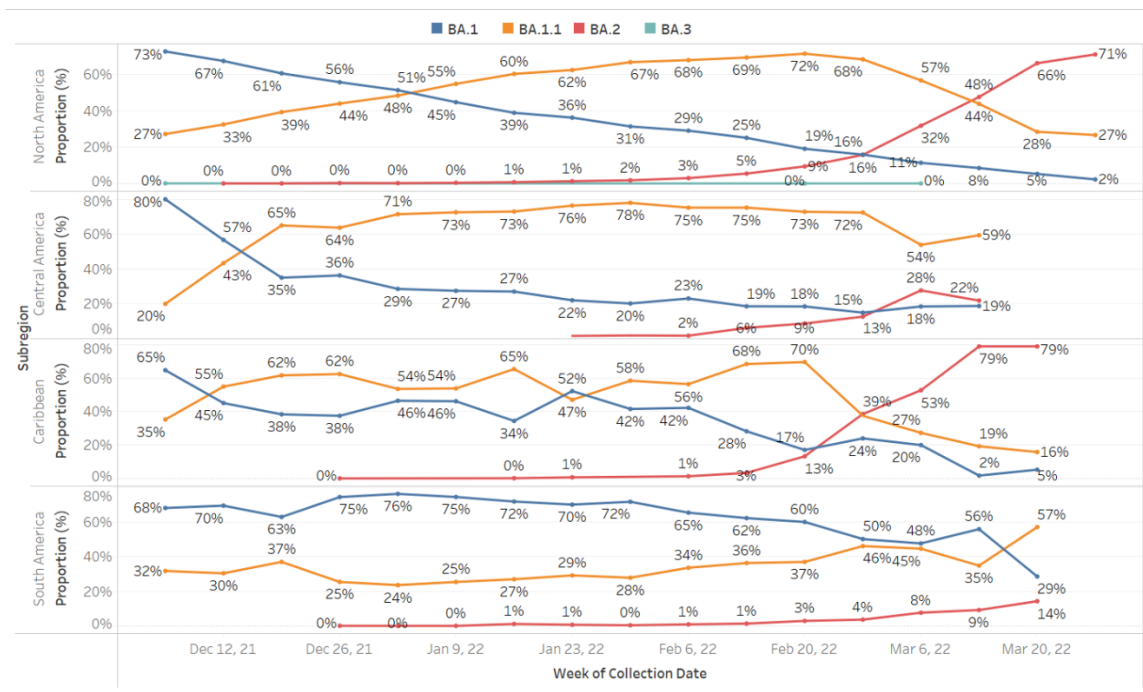
¹ Operational definitions that are periodically reviewed and updated as necessary. WHO. Tracking SARS-CoV-2 variants. Available at: <https://bit.ly/36FXgQY>

Regardless of these additional mutations and emergence of new sublineages, no significant changes in public health impact regarding the Omicron sublineages have been demonstrated, besides the high transmission capacity already demonstrated by Omicron. Although some treatments based on monoclonal antibodies might be affected by specific structural changes, vaccination, and non-pharmacological measures, including appropriate use of masks, remain extremely useful to control the virus and surge of cases.

Phylogeny and global distribution of VOC Omicron by sample collection date (up to 10 April 2022)



Circulation of Omicron sublineages at PAHO Region (December 2021 to March 2022)



Recombination events

Genetic recombination is a natural phenomenon already described in different viruses as a mutation mechanism to exchange genomic material (which is different from the reassortment mechanism observed in segmented genomes such as that of influenza).

On 8 February 2022, a recombination event between the variants of concern (VOC) Delta and Omicron was reported in Europe. Although the event was described for the first time in France, it is not clear yet where the first emergence of the recombinant occurred. The virus sequence indicates mainly Delta genes (sublineage AY.4) with most of the Spike protein gene (S) corresponding to Omicron (sublineage BA.1).

Similar recombinants (currently denominated XD) were documented in clusters reported in Denmark and the Netherlands, as well as in isolated cases in Belgium and Germany. It is not yet clear if these viruses derive from a common ancestor or if they correspond to different recombination events.

On the other hand, the simultaneous high circulation of BA.1 and BA.2 has facilitated the occurrence of recombination between these 2 sublineages and the event has already been demonstrated in different countries including the United Kingdom where at least 6 different recombinants have been described (depending on the recombination sites), denominated XE, XR, XL, XN, XP and XQ with XE the most detected at the country level. Denmark (XG, XH), Finland (XJ), Belgium (XK), and Netherlands (XM), have also detected additional recombination events. Also, signals that remain to be confirmed have been reported in Costa Rica (possible XE)

Currently, there is no evidence that indicates a significant increased transmission capacity, or changes in the clinical form or severity of the disease due to infection with this recombinant virus, and all public health control measures including vaccines remain highly efficient and should be maintained. Also, the recommendation to maintain and enhance genomic surveillance for the early detection of any change in viral sequences and viral behavior is reiterated.

Guidance for national authorities

PAHO/WHO reiterates to Member States the need to: (i) maintain genomic surveillance activities; (ii) ensure the immediate publication of genomic sequences produced on the GISAID platform (www.gisaid.org); and (iii) immediately report the first detection of infections identified as a variant of concern (VOC), according to the following WHO document: <https://bit.ly/3sd4Psb>.